WO 99/25727

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EXENDIN-3

His Ser Asp Gly Thr Phe Thr Ser Asp Leu Ser Lys Gln Met Glu Glu 1 5 10 15 Glu Ala Val Arg Leu Phe Ile Glu Trp Leu Lys Asn Gly Gly Pro Ser 20 25 30 Ser Gly Ala Pro Pro Pro Ser-NH,

Fig. 1

EXENDIN-4

His Gly Glu Gly Thr Phe Thr Ser Asp Leu Ser Lys Gln Met Glu Glu
5 10 15

Glu Ala Val Arg Leu Phe Ile Glu Trp Leu Lys Asn Gly Gly Pro Ser
20 25 30

Ser Gly Ala Pro Pro Pro Ser-NH,
35

Fig. 2

$GLP-1 (GLP-1[7-36]NH_2)$

His Ala Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly 5 10 15 Gln Ala Ala Lys Glu Phe Ile Ala Trp Leu Val Lys Gly Arg-NH $_2$ 20 25 30

Fig. 3



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osition	g 29	d 37	d 38	65 P	d 40	d 41	d 42	d 43	d 44	d 45	d 46	47 P	d 48	d 49	92	d 51	d 52	3	충	d 55	929	2 2	<u>8</u>	22	8	ड्डी
Amino Acid Position	Compound 36 His Gly Glu Gly Thr Phe	Compound 37 His Gly Glu Gly Thr Phe	Compound 38 His Gly Glu Gly Thr Phe	Compound 39 His	Compound 40 His	Compound 41 His Gly Glu Gly Thr Phe	Compound 42 His Gly Glu Gly Thr Phe	Compound 43 His Gly Glu Gly Thr Phe	Compound 44 His Gly Glu Gly Thr Phe	Compound 45 His Gly Glu Gly Thr Phe	Compound 46 His Gly Glu Gly Thr Phe	Compound 47 His Gly Glu Gly Thr Phe	Compound 48 His Gly Glu Gly Thr Phe	Compound 49 Arg Gly Glu Gly Thr Phe	Compound 50 His Gly Asp Gly Thr Phe	Compound 51 His Gly Glu Gly Thr naph Thr Ser Asplteu	Compound 52 His Gly Glu Gly Thr Phe	Compound 53 His	Compound 54 His Gly Glu Gly Thr Phe	Compound 55 His Gly Glu Gly Thr Phe	Compound 56 His Gly Glu Gly Thr Phe	Compound 57 His Gly Glu Gly Thr Phe	Compound 58 His Gly Glu Gly Thr Phe	Compound 59 His Gly Glu Gly Thr Phe	Compound 60 His Gly Glu Gly Thr Phe	Compound 61 His Gly Glu Gly Thr Phe
Amtho	స్త	ဦ	ဦ	ဉ်	ঠ	ဦ	S	S	ဦ	S	S	Con	Cod	Son	S	S	S	S	S	ပ္ပ	Š	ફ	န	ठ	န	5

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04/09

Glucose lowering effect in db/db mice at 1 hr time point

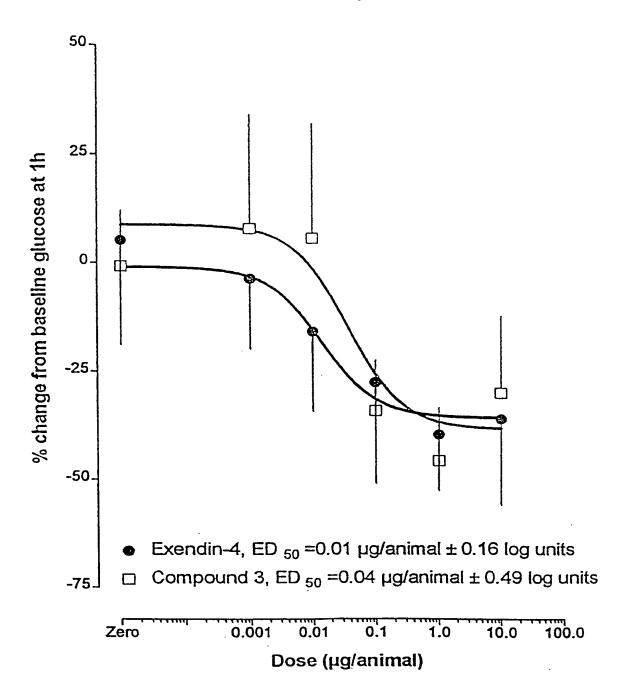
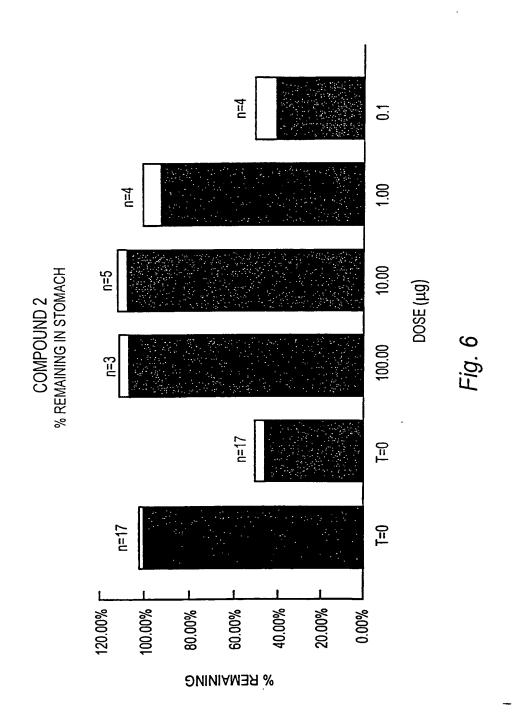
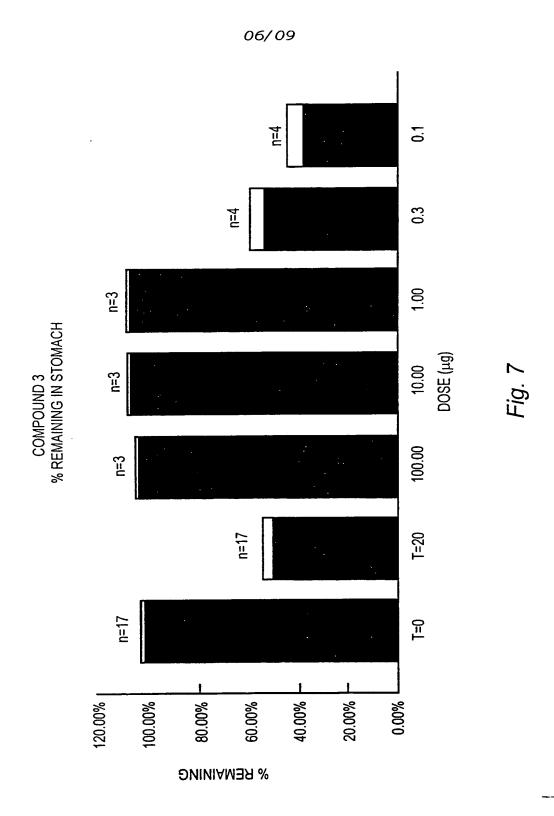


Fig. 5
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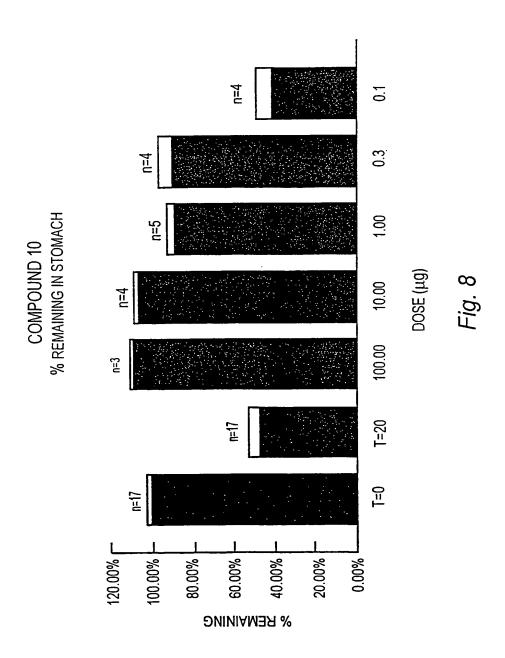


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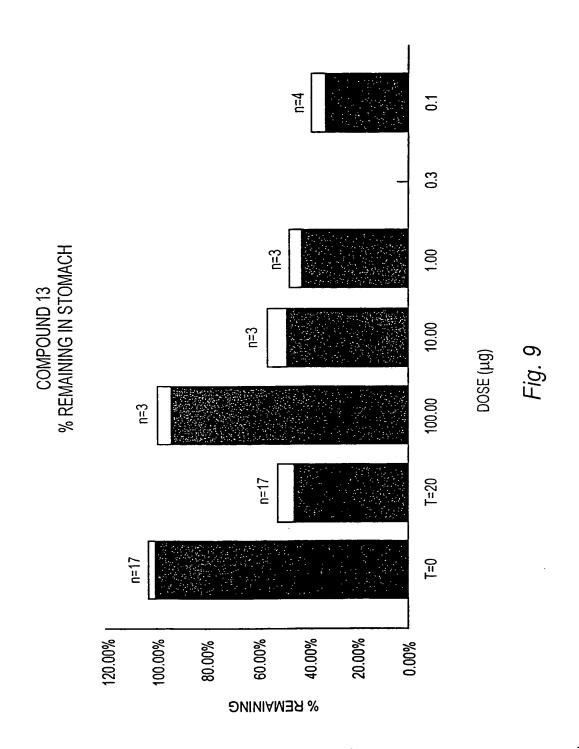
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Compound

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09/09 4-Imidazolylpropionyl-Gly Glu Gly Thr Phe Thr Ser Asp Leu Ser Lys Gln Met Glu Glu Glu Ala Val Arg Leu 4-Imidazolylpropionyl-Gly Glu Gly Thr Phe Thr Ser Asp Leu Ser Lys Gln Leu Glu Glu Glu Ala Val Arg Leu 4-Imidazolylpropionyl-Gly Glu Gly Thr Phe Thr Ser Asp Leu Ser Lys Gln Met Glu Glu Glu Ala Val Arg Leu 4-Imidazolylpropionyl-Gly Glu Gly Thr Phe Thr Ser Asp Leu Ser Lys Gln Leu Glu Glu Glu Ala Val Arg Leu 4-Imidazolylpropionyl-Gly Glu Gly Thr Phe Thr Ser Asp Leu Ser Lys Gln Met Glu Glu Glu Ala Val Arg Leu 4-Imidazolylpropionyl-Gly Glu Gly Thr Phe Thr Ser Asp Leu Ser Lys Gln Met Glu Glu Glu Ala Val Arg Leu 4-Imidazolylpropionyl-Gly Glu Gly Thr Phe Thr Ser Asp Leu Ser Lys Gln Leu Glu Glu Glu Ala Val Arg Leu 4-Imidazolylpropionyl-Gly Glu Gly Thr Phe Thr Ser Asp Leu Ser Lys Gln Leu Glu Glu Glu Ala Val ID NO. 70] 73] 69] 74] [SEQ. [SEQ. ID NO. ID NO. ID NO. 71] 72] 67] Arg Leu Phe Ile Glu Phe Leu Lys-NH'octanoyl Asn Gly Gly-NH, [SEQ. [SEQ. (SEQ. ID NO. [SEQ. ID NO. ID NO. ID NO. Phe Ile Glu Phe Leu Asn Lys-NH°octanoyl Gly Gly-NH, Phe Ile Glu Trp Leu Lys-NH'octanoyl Asn Gly Gly-NH2 Phe Ile Glu Trp Leu Asn Lys-NH'octanoyl Gly Gly-NH, SEQ. [SEQ. Phe Ile Glu Trp Leu Lys-NH'octanoyl Asn-NH, Phe Ile Glu Phe Leu Lys-NHtoctanoyl Asn-NH, Phe Ile Glu Trp Leu Asn Lys-NHtoctanoyl-NH, Phe Ile Glu Phe Leu Asn Lys-NH'octanoyl-MH, 65 99 67 69 62 63 64 68